2 needs

4. (Twice Amended) The sustained release pharmaceutical formulation of claim 1 wherein said formulation provides a time to peak plasma concentration (T_{max}) of the metformin which occurs at a time from about 8 hours to about 12 hours after administration to said human patient.

3

30. (Amended) The sustained release pharmaceutical formulation of claim 1 wherein said metformin or pharmaceutically acceptable salt thereof is metformin hydrochloride.

4

32. (Amended) The sustained release dosage form of claim 31, which provides an increase in the bioavailability of said metformin if taken with food.

REMARKS

Reconsideration of this application in view of the following remarks is respectfully requested. Claims 1-4, 6-20 and 24-34 are pending. Claim 5 has been cancelled and claims 1, 3, 4, 30, and 32 have been amended without prejudice.

I. Rejections Under 35 U.S.C. §103(a)

In the Office Action, claims 1-20 and 24-34 were rejected under 35 U.S.C. §103(a) as being as being "unpatentable over Bhagwat et al. (U.S. 6,056,977)".

In the Office Action, the Examiner states the following

> In response to the argument that hypoglycemic drug is not antihyperglycemic is not persuasive because hypoglycemic drug does the same function as antihyperglycemic drug. Bhagwat specifically lists metformin as hypoglycemic drug and metformin is an antihyperglycemic drug as acknowledged and claimed by applicants," and "Bhagwat discloses that metformin, butformin, glipzide and phenformin are formulated as controlled release dosage forms. The argument that the formulation of the instant application releases the antihyperglycemic drug over a period of 12-24 hours is not persuasive because the application broadly claims pharmaceutical composition comprising

> an antihyperglycemic drug or a pharmaceutically acceptable salt thereof. Intended use is not critical in a composition claim. In the absence of a showing of unexpected result, once a day dosing or release of the active agent over a period of 12-24 hours is not inventive over the prior art. There is nothing in the composition that differs from the prior art that affords the composition of the application the property claimed and there is no showing that the composition of the prior art would not have that property. If there is one, applicants have not presented the difference. It is not enough to say that a composition comprising A, B and C releases C over a period of 12-24 hours, and another composition comprising A, B, and (C or D or E or F) would not release C over a period of 12-24 hours. What is the criticality of the 12-24 hours of the application over the formulation of the prior art.

In addition, the Examiner summarizes that rejection of the previous Office Action, stating that ". . .applicants did not address merits of demerits of the rejection on record in the response filed on 04/11/02 and 04/26/02 . . . ."

This rejection is traversed. It is respectfully submitted that contrary to the Examiner's statements, a hypoglycemic drug is not the same as a antihyperglycemic drug and does not function in the same manner. (*See, e.g*, Glucophage, Physician's Desk Reference, 2002, page 1080, under Clinical Pharmacology section). Further, contrary to the Examiner's assertion, Bhagwat does not list metformin as a hypoglycemic drug. In the description of U.S. Patent No. 6,056,977 to Bhagwat et al. (hereinafter "Bhagwat"), the only reference made to metformin is in the "Background of the Invention" in column 3, lines 4 to 11, wherein "methformin" (sic) is referred to as an "antidiabetic agent". Although Bhagwat does recite "phenformin" (another antihyperglycemic drug) in the "Background of the Invention" at column 2, line 65, there is no teaching, hint or suggestion of the use of phenformin or any other antihyperglycemic drug in the formulations of Bhagwat. However, for the purposes of advancing the prosecution of the present application, the term "antihyperglycemic agent" has been removed from the claims in favor of metformin or pharmaceutically acceptable salt thereof.

It is respectfully submitted that Bhagwat is directed to controlled release sulfonylurea antidiabetic formulations. As indicated in the "Background of the Invention" of Bhagwat ". . . sulfonylureas are relatively insoluble and therefore inherently difficult to be solubilized from an oral dosage form in the gastrointestinal tract and then be absorbed through the walls of the gastrointestinal tract" (Column 4, lines 6-11), and in the "Summary of the Invention" Bhagwat indicates that the invention is directed to "a controlled release sulfonylurea antidiabetic formulation that is suitable for once-a-day or 24 hour administration and that is formulated into a solid sustained release matrix that includes an alkalizing medium affording substantially complete bioavailability from the sustained release matrix." (Column 4, lines 28-33).

It is respectfully submitted that metformin or its pharmaceutically acceptable salts are not sulfonylureas (in support of this statement, see Facts and Comparisons, 1999, page 635, first paragraph, which is enclosed herewith) and Bhagwat fails in the very least to teach, hint, or suggest sustained release oral dosage forms comprising metformin or a pharmaceutically acceptable salt thereof .

Furthermore, in contrast to sulfonylureas, metformin is freely soluble. One of ordinary skill in the art would not use the teachings of Bhagwat which describes sulfonylureas, which are relatively insoluble agents, to prepare a sustained release pharmaceutical formulation comprising metformin, which is a freely soluble antihyperglycemic agent. In addition, it is respectfully submitted that one of ordinary skill would not be motivated to prepare controlled release metformin formulations in view of Bhagwat, as the problems associated with the decreased solubility of the sulfonylureas of Bhagwat would not be encountered with metformin which is freely soluble.

II. Double Patenting

In the Office Action, claims 1-20 and 24-34 remained rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent Nos. 6,099,859. Further, claims 1-20 and 24-34 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-54 of copending Application No. 09/594,637.

In response, and solely to expedite prosecution of this application, Applicants submit herewith two terminal disclaimers. Applicants maintain their position that these terminal disclaimers are not necessary and note that the obviation of an obvious-type double patenting rejection by the filing of a terminal disclaimer is not an admission, acquiescence, or estoppel on the merits of an issue of obviousness. *See Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 873-74, 20 U.S.P.Q.2d 1392, 1394-95 (Fed. Cir. 1991).

The Assistant Commissioner is authorized to charge Deposit Account No. 50-0552 for $220.00 which covers the fees for the two terminal disclaimers. If any additional fees are deemed to be due at this time, the Assistant Commissioner is authorized to charge payment of the same to Deposit Account No. 50-0052.

III. Conclusion

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "**Version With Markings To Show Changes Made**."

It is now believed that the above-referenced rejections and objections have been obviated and it is respectfully requested that the rejections and objections be withdrawn. It is believed that all claims are now in condition for allowance.

According to currently recommended Patent Office policy the Examiner is specifically authorized to contact the undersigned in the event that a telephonic interview will advance the prosecution of this application.

An early and favorable action is earnestly solicited.

Respectfully submitted,

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By: _____

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Version With Markings To Show Changes Made

1. (Amended) A sustained release pharmaceutical formulation comprising **[an antihyperglycemic drug]** **metformin** or a pharmaceutically acceptable salt thereof, wherein said formulation provides therapeutic plasma levels of said antihyperglycemic drug to a human patient over a 24 hour period after administration to said patient.

3. (Amended) The sustained release pharmaceutical formulation of claim 1 wherein the bioavailability of the **[antihyperglycemic drug]** **metformin** is increased by the presence of food.

4. (Twice Amended) The sustained release pharmaceutical formulation of claim 1 wherein said formulation provides a time to peak plasma concentration (T_{max}) of the **[antihyperglycemic drug]** **metformin** which occurs at a time from about 8 hours to about 12 hours after administration to said human patient.

30. (Amended) The sustained release pharmaceutical formulation of claim 1 wherein said **[antihyperglycemic drug]** **metformin or pharmaceutically acceptable salt thereof** is metformin hydrochloride.

32. (Amended) The sustained release dosage form of claim 31, which provides an increase in the bioavailability of said **[antihyperglycemic drug]** **metformin** if taken with food.